**REMARKS**

Claims 1 and 5 are pending in the instant application. Claims 1 and 5 have been rejected. Claim 5 has been amended. No new matter has been added by this amendment. Reconsideration is respectfully requested in light of the following remarks.

**I. Related Applications**

The filing date for CA 2,362,787 and EP 00913470.1 is February 15, 2000.

**II. Withdrawn Objections/Rejections**

Applicants acknowledge withdrawal of the objection of the Disclosure for the typographical error on page 5 and the rejection under 35 U.S.C. 112, first paragraph, based on enablement.

Applicants acknowledge that the obviousness-type double patenting rejection in the last Office Action was a provisional rejection.

**III. Rejection Under 35 U.S.C. 112**

Claims 1 and 5 have been rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicants regard as the invention with respect to the recitation "specific redox state". It is suggested that the specification does not provide a standard for ascertaining the scope of "specific redox state". Applicants respectfully traverse this rejection.

MPEP 2173.05(b) states that "The fact that claim language, including terms of degree, may not be precise, does not automatically render the claim indefinite under 35 U.S.C. 112, second paragraph. *Seattle Box Co., v. Industrial Crating & Packing, Inc.*, 731 F.2d 818, 221 USPQ 568 (Fed. Cir. 1984). Acceptability of the claim language depends on whether one of ordinary skill in the art would understand what is claimed, in light of the specification.

The specification clearly teaches at page 5, lines 5-17, that a redox clamping agent can adjust and maintain the relative amount of cellular constituents such that a specific redox condition is sustained to facilitate the action of the therapeutic agent. It is further disclosed at page 8, lines 34, to page 9, lines 11, that the specific redox state is defined by the levels of cellular GSH, MT and other redox-defining molecules which correlate with indicators of tumor differentiation and proliferation (*e.g.*, PSA mRNA levels, Bcl-2/Bax ratio, and proliferation indices). Accordingly, one of skill would appreciate that the specific redox state, as defined by these various factors, can vary. Thus, as Applicants have provided the necessary guidance to one of skill in the art for determining the specific redox state as defined by the factors associated therewith, it is respectfully requested that this restriction be reconsidered and withdrawn.

**IV. Rejection Under 35 U.S.C. 102**

Claim 5 has been rejected under 102(a) as being anticipated by Obrosova et al. (1998) *Diabetologia* 41:1442-1450. It is suggested that in teaching a diabetic model wherein a

stabilization of lenticular cells contacted with a thiol-containing molecule, α-lipoic acid, is demonstrated, Obrosova et al. anticipate the instant invention. Applicants respectfully disagree.

As disclosed at page 3, lines 14-19 and page 11, lines 1-2, Applicants' invention is a method of stabilizing the redox state of hyperproliferative cells with abnormal fluctuations in their redox state (*e.g.*, epidermal cells of psoriasis) by contacting the cells with a redox clamping agent comprising a thiol(sulfhydryl)-containing molecule. While Obrosova et al. disclose the use of rats with 6-week streptozotocin-induced diabetes and the effect of alpha-lipoic acid on lens antioxidant status, glucose utilization, redox state of free cytosolic NAD(P)-couples and adenine nucleotides, this reference does not teach or suggest the use of alpha-lipoic acid to stabilize the redox state of *hyperproliferative* cells with abnormal fluctuations in their redox state. Thus, in an effort to highlight this feature of Applicants' invention, claim 5 has been amended to clarify that the cells being contacted with the thiol(sulfhydryl)-containing molecule are *hyperproliferative* cells. As Obrosova et al. fail to teach each and every element of the amended claim, this reference does not anticipate the present invention. It is therefore respectfully requested that this rejection be withdrawn.

Claim 1 has been rejected under 35 U.S.C. 102(e) as being anticipated by Demopoulos et al., US 2002/0136763. It is suggested that in teaching cells contacted with a chemotherapeutic agent and a redox clamping agent that is a thiol-containing molecule, *i.e.*, glutathione, wherein a desired

redox state is maintained, Demopoulos et al. anticipate the instant invention. Applicants respectfully traverse this rejection.

Applicants respectfully disagree with the Examiner's interpretation of the teachings of the cited reference. Paragraph [0017] cited by the Examiner states that GSH "has been used as an adjunct therapy to treatment with nephrotoxic chemotherapeutic agents such as cisplatin, and has been reported to prevent doxorubicin-induced cardiomyopathy." Further, paragraph [0022] cited by the Examiner, teaches that oxidative stresses, *i.e.*, low intracellular levels of reduced GSH, and relatively high levels of free radicals, activate cellular transcription and translation and that RNA viral or retroviral replication requires a relatively oxidized state of the cell, a condition which results from stress, low glutathione levels, or the production of reduced cellular products. While paragraph [0022] further indicates that by maintaining a relatively reduced state of the cell (redox potential), viral transcription is impeded, this reference is silent to the effect of maintaining cells in a specific redox state in the presence of a chemotherapeutic agent and a thio(sulfhydryl)-containing molecule. The skilled artisan would appreciate that tumor development and viral infection are very different pathologies and this reference fails to teach or suggest that glutathione is having the same effect in both types pathologies. Further, while this reference claims the administration of stabilized glutathione in combination with a cancer chemotherapeutic agent such as cisplatin, doxorubicin, and daunorubicin, the use of glutathione in combination with chemotherapeutic agents is taught in the cited reference as

*adjunct therapy, e.g.,* to prevent doxorubicin-induced cardiomyopathy or reduce systemic toxicity of agents such as cisplatin (see paragraphs [0022] and [0072]. This reference does not teach or suggest the combination of a chemotherapeutic agent and a thio(sulfhydryl)-containing molecule as the primary mode of treatment in accord with the instant claims to sensitize cells to the chemotherapeutic agent. Therefore, because this reference fails to teach each and every element of the claim, this reference does not anticipate the present invention. It is therefore respectfully requested that this rejection be withdrawn.

**V. Conclusion**

The Applicants believe that the foregoing comprises a full and complete response to the Office Action of record. Accordingly, favorable reconsideration and subsequent allowance of the pending claims is earnestly solicited.

Respectfully submitted,

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Date: **April 25, 2005**

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